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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Before the Board of Patent Appeals and Interferences

In re Appeal regarding Patent Application of	:	
Applicants : LINCOLN, Stephen E. and KNAPP, Michael R.	:	Examiner: FREDMAN, Jeffrey N.
Serial No. : 09/618,178	:	Art Unit 1637
Filed : 18 July 2000	:	
Title : Automatic Genotype Determination	:	

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REPLY BRIEF

A. Rebuttal

In the present rebuttal, it will not be attempted to point out each and every error in the Examiner's Answer of 5 February 2007, particularly since many of the positions taken in the Examiner's Answer were essentially repeated from the final Office Action of 12 October 2005 on appeal and have been fully discussed in the Appeal Brief of 17 November 2006. Generally only the more fundamental errors in new points raised in the Examiner's Answer will be discussed in the present rebuttal.

A.1 The Rejections Under 35 U.S.C. § 103(a)

A.1.a New Claim Chart Highlights Errors

A fundamental error which underlay the unwarranted rejections under 35 U.S.C. § 103(a) in the final Office Action of 12 October 2005 on appeal and which was highlighted in a new claim chart in the Examiner's Answer of 5 February 2007 was the failure to recognize the distinction between carrying out certain statistical operations on reaction values indicative of the presence of a particular allele at a locus within genetic material obtained from a subject as called for by the claims of the subject application and carrying out necessarily fundamentally-different statistical operations on either the frequencies or aggregate numbers of previously-determined genotypes and constituent alleles exhibited in a sample of individuals randomly selected from a population of individuals to estimate the extent to which the population exhibited or departed from Hardy-Weinberg equilibrium. Such error is evident, for example, in the second, lower pair of boxes of the claim chart on page 11 of the Examiner's Answer and the first, uppermost pair of boxes of the claim chart on page 12.

In the second, lower pair of boxes of the claim chart on page 11 of the Examiner's Answer it was asserted that a limitation "B" of claim 75 of the subject application:

"forming a data set including the first reaction value;"

[underlining added] corresponded literally to the following passage from page 17, column 1 of the Kimpton *et al.* publication:

> Allele frequencies for each STR locus under investigation were determined from a minimum of 50 random individuals for each of three different populations: Caucasians, Afro-Caribbeans, and Asians. Allele frequency histograms for all 14 loci are shown in Figure 3. Symmetrical and skew unimodal, bimodal and more complex distributions were observed among the 14 loci. Differences in allele frequencies among population groups were also seen.

[Underlining added.] Regarding the "allele frequency histograms" referred to in the quoted passage from the Kimpton *et al.* publication, reference to the caption of Figure 3 on page 18 of the publication will reveal that the x-axis of the allele frequency histograms of the Figure represented an "allele designation number" and the y-axis of the histograms represented an allele frequency. The allele designation number on the x-axis of the allele frequency histograms constituted a name designating a particular short-tandem-repeat allele, not an experimental electrophoretic band size. Thus a process of assigning named allele designations for each of the random individuals of the three populations based on measured electrophoretic band size measurements had to have been carried out prior to compiling the allele frequency data plotted in Figure 3 of the Kimpton *et al.* publication. It is submitted, as discussed in more detail below and in the Appeal Brief, that the Kimpton *et al.* publication does not disclose, suggest, or motivate, but affirmatively teaches away from, the method of claim 75 of the subject application for determining the genotype of a subject at a locus. Moreover, as persons of ordinary skill in the art would have recognized as of the effective filing date of the subject application, it would not have been possible to deconstruct an allele frequency histogram of Figure 3 of the Kimpton *et al.* publication to retrieve a particular measured electrophoretic band size for a particular individual who had been assigned a given allele designation number on the basis of a measured electrophoretic band size. It is submitted therefore that, contrary to the assertion in the Examiner's Answer, the passage from the Kimpton *et al.* publication referring to determination of allele frequencies for each of 14 short-tandem-repeat loci from a minimum of 50 random individuals for each of three different populations quoted in the lower left-hand box of the claim chart on page 11 of the Examiner's Answer did not disclose forming a data set including a first

reaction value as called for in step "B" of claim 75 of the subject application even assuming for the sake of argument that measured electrophoretic band sizes of the analytical method disclosed in the Kimpton *et al.* publication constituted reaction values.

In the uppermost, first pair of boxes of the claim chart on page 12 of the Examiner's Answer it was asserted that a limitation "C" of claim 75 of the subject application:

> "establishing a distribution set of probability distributions, including at least one distribution, associating hypothetical reaction values with corresponding probabilities for each genotype of interest at the locus;"

[underlining added] corresponded literally to the following passage from page 17, column 2 of the Kimpton *et al.* publication:

> The data sets were tested for Hardy-Weinberg equilibria using a log likelihood-G test. In total, 42 locus population comparisons were carried out. Deviation from Hardy-Weinberg equilibria was only detected for the HUMC-YARO3 Caucasian data ($P<0.05$).

[Footnote omitted.] Persons of ordinary skill in the art would have understood that the data sets referred to in the preceding quoted passage from the Kimpton *et al.* publication were sets of the allele frequency data plotted as histograms in Figure 3 and corresponding genotype frequency data, in view of the context in the publication of the quoted passage which immediately followed a paragraph concerning determining allele frequencies for at least 50 random individuals for each of three different populations, in view of the reference to "42 locus population comparisons," which corresponded to 14 loci times 3 populations; and in view of the nature of tests for Hardy-Weinberg equilibrium as discussed in more detail below and in the Appeal Brief. There was no indication in the Kimpton *et al.* publication that the data sets referred to in the quoted passage included or could be deconstructed to retrieve a particular measured electrophoretic band size for a particular individual who had been assigned a given allele designation number or a given allele-pair heterozygous genotype designation or a given single-allele homozygous genotype designation on the basis of measured electrophoretic band sizes. It is submitted therefore that,

contrary to the assertion in the Examiner's Answer, the passage from the Kimpton *et al.* publication referring to testing certain data sets for Hardy-Weinberg equilibria quoted in the uppermost left-hand box of the claim chart on page 12 of the Examiner's Answer did not disclose establishing a distribution set of probability distributions associating hypothetical reaction values with corresponding probabilities for each genotype of interest at a locus as called for in step "C" of claim 75 of the subject application even assuming for the sake of argument that measured electrophoretic band sizes of the analytical method disclosed in the Kimpton *et al.* publication constituted reaction values.

A.1.b Assertion that Hardy-Weinberg Equilibrium Analysis Employed in the Kimpton *et al.* Publication is Necessary for the Claims is Erroneous

In the paragraph bridging pages 13 and 14 of the Examiner's Answer, it was asserted that "the use by Kimpton of the Hardy-Weinberg equilibrium analysis is precisely the analysis necessary for the claims and necessary to determine the allelic information of a particular individual." It is submitted that the assertion to the effect that Hardy-Weinberg equilibrium analysis as employed in the Kimpton *et al.* publication is necessary for the claims of the subject application and necessary to determine the allelic information of a particular individual is fundamentally incorrect, as demonstrated in the following paragraphs.

Independent claim 75 of the subject application, for example, is directed to a method for determining the genotype of a subject at a genetic locus within genetic material obtained from a biological sample from the subject which includes a step, among others, of establishing a distribution set of probability distributions associating hypothetical reaction values with corresponding probabilities for each genotype of interest at the locus. The method of claim 75 further includes the steps of reacting the material at the locus to obtain a first reaction value indicative of the presence of a given allele at the locus and applying the first reaction value to each pertinent probability distribution to determine a measure of a conditional probability of each genotype of interest at the locus. The method of claim 75 includes a final step of determining the genotype based on data from the step of applying the first reaction value to each

pertinent probability distribution. By its terms, the method of claim 75 does not require any information concerning the frequency of occurrence over a population of the various genotypes and alleles associated with a genetic locus. However, genotype and allele frequency-of-occurrence-over-a-population information is the sort of information involved in an analysis for Hardy-Weinberg equilibrium. It is submitted therefore that the assertion quoted above from the Examiner's Answer that "the use by Kimpton of the Hardy-Weinberg equilibrium analysis is precisely the analysis necessary for the claims" is fundamentally incorrect.

Moreover, concerning analysis for Hardy-Weinberg equilibrium, as explained on pages 15 and 16 of the Appeal Brief of 17 November 2006, it is submitted that persons of ordinary skill in the art would have understood such analysis to involve ascertaining either the frequencies or aggregate numbers of genotypes and constituent alleles exhibited in a sample of individuals randomly selected from a population of interest and comparing in some way the observed frequencies of the various genotypes exhibited in the sample to the corresponding "expected" genotype frequencies computed from the frequencies of alleles exhibited in the sample using the set of algebraic relations which define Hardy-Weinberg equilibrium to make a judgment about the extent to which the overall population of interest exhibits or departs from Hardy-Weinberg equilibrium. A test for Hardy-Weinberg equilibrium would ordinarily take as original input data, data enumerating aggregate numbers of genotypes and constituent alleles exhibited in a population sample based on previously obtained genotype identifications for members of the sample. The method by which genotype identifications are made for individuals in a population would in no way affect how a test for Hardy-Weinberg equilibrium is carried out. Moreover, a test for Hardy-Weinberg equilibrium would not provide any output information which could be used by itself to determine the particular genotype of any individual from the population. Carrying out statistical operations on either the frequencies or aggregate numbers of previously-determined genotypes and constituent alleles exhibited in a sample of individuals randomly selected from a population of individuals to estimate the extent to which the population exhibited or departed from Hardy-Weinberg equilibrium therefore differs fundamentally from the operations involving reaction values indicative of the presence of a particular allele at a locus

within genetic material obtained from a subject to determine the genotype of the subject as called for by claim 75 of the subject application. It is submitted therefore that the assertion quoted above from the paragraph bridging pages 13 and 14 of the Examiner's Answer to the effect that Hardy-Weinberg equilibrium analysis as employed in the Kimpton *et al.* publication is necessary to determine the allelic information of a particular individual is fundamentally incorrect.

A.1.c Calculation of Matching Probabilities Would Not Have Suggested Any Modification in the Method of the Kimpton *et al.* Publication

In the second full paragraph on page 14 of the Examiner's Answer, it was asserted that Table 4 of the Kimpton *et al.* publication disclosed the results of a matching probability analysis and a reference to calculating matching probabilities, denoted pM, on page 15, column 1 of the publication was noted. It is submitted that persons of ordinary skill in the art would have recognized that the probability of a match conventionally referred to the probability that two unrelated individuals selected randomly from a population would have exactly the same genotype with respect to one or more genetic loci. It is submitted further that persons of ordinary skill in the art would have recognized that calculation of a probability of a match with respect to a population and a set of one or more genetic loci entailed selecting a random sample of individuals from the population and determining the genotypes of the sampled individuals to estimate the frequency over the population of the various alleles associated the set of loci. Results of a probability of a match calculation would not have been used in connection with determining the genotype of an individual in the first instance. That the Kimpton *et al.* publication disclosed the calculation of conventional matching probabilities would not have suggested to a person of ordinary skill in the art any modification or change in the analytical method of the publication.

A.1.d No Motivation to Modify the Method the Kimpton *et al.* Publication for Precise Allele Designation

In the Appeal Brief of 17 November 2006 it was pointed out that, in the analytical method disclosed in the Kimpton *et al.* publication, short-tandem-repeat loci with tri- and

tetrameric repeats were deliberately selected in order to permit precise, unambiguous allele designation using polyacrylamide gels with automated fluorescence-based technology and that therefore a person of ordinary skill using the analytical method disclosed in the publication would have had no motivation to modify the method to determine allele sizes by some other procedure as proposed in the final Office Action on appeal. In the paragraph bridging pages 14 and 15 of the Examiner's Answer, the observation in the Appeal Brief that the accuracy of measuring allele values in the method disclosed in the Kimpton *et al.* publication eliminated any motivation to modify the method was acknowledged, but it was asserted that nonetheless the publication included two disclosures which assertedly would have suggested modifying the method of the publication. It is demonstrated below that, when read in context, the two asserted suggestions to modify the analytical method of the Kimpton *et al.* publication in fact support the position that a person of ordinary skill would have had no motivation to use any method to determine allele sizes other than the method disclosed in the publication.

It was asserted on page 15 of the Examiner's Answer that the following statement from page 20, column 3 of the Kimpton *et al.* publication would have taught that, in forensic applications, additional statistical analysis was necessary to distinguish artifactual stutter bands:

> The overall pM of the three multiplex systems developed was $<1 \times 10^{-14}$, thus highlighting the power of theses systems for individual identification. However, before a discriminatory system is accepted for routine forensic use, it must be proved to be both robust and reliable. The high incidence of artifactual stutter bands observed with dinucleotide STR loci make them unsuitable for forensic applications.

However, the discussion concerning the suitability of the analytical method of the Kimpton *et al.* publication for forensic applications at page 20, column 3 of the publication was truncated in the Examiner's Answer in a way that omitted the solution disclosed in the publication to the problem of artifactual stutter bands observed with ***di***nucleotide short-tandem-repeat loci referred to in the truncated quotation. Immediately following the truncated quotation offered in the Examiner's

Answer as a suggestion to modify the method of the Kimpton *et al.* publication is the following disclosure:

> However, the significantly reduced level of stuttering for 3- to 5-bp repeat loci observed both in this and previous studies, suggests that these STRs are more amenable to forensic investigations. This is reinforced by preliminary studies carried out in our laboratories on forensic material (data not shown).

[Footnote omitted.] Thus, read in its entirety, the discussion at page 20, column 3 of the Kimpton *et al.* publication concerning forensic applications of the analytical method of the publication reiterates and confirms other disclosures in the publication that, in the analytical method of the publication, short-tandem-repeat loci with three or four base-pair repeat units could be selected to permit precise, unambiguous allele designation using polyacrylamide gels with automated fluorescence-based technology and that the allele-designation method disclosed in the publication provided all the resolution and accuracy needed in the automated DNA profiling system of the publication. For a discussion of disclosures in the Kimpton *et al.* publication of the sufficient accuracy of the allele-designation method disclosed in publication for its disclosed purpose in addition to the disclosure concerning forensic applications at page 20, column 3 of the Kimpton *et al.* publication, see pages 21 through 24 of the Appeal Brief of 17 November 2006.

In a sentence bridging pages 14 and page 15 of the Examiner's Answer, it was asserted that the Kimpton *et al.* publication at page 20, column 2 disclosed that certain alleles were not as easily analyzed as others and, according to the Examiner's Answer, would have "require[ed] analysis of the distributions." In the first partial paragraph of column 2 of page 20 of the Kimpton *et al.* publication, with reference to the two short-tandem-repeat loci respectively designated HUMAPOAI1 and HUMACTBP2, it was stated:

> Prior to routine use of these loci by forensic laboratories for the identification of individuals, it must be confirmed that the

> detection and sizing protocols used allow accurate, reliable, and unambiguous allele designation.

Following the preceding quotation at the end of the first partial paragraph of column 2 on page 20 of the Kimpton *et al.* publication was a second paragraph which made no mention of the two loci designated HUMAPOAI1 and HUMACTBP2, but concerned solely a third locus designated D21S11. Following the second paragraph of column 2 on page 20 of the publication was a third paragraph which made no mention of any particular locus, and in particular made no mention of any of the short-tandem-repeat loci designated HUMAPOAI1, HUMACTBP2, or D21S11 referred to in the preceding paragraphs of column 2 of page 20. The third paragraph beginning in column 2 of page 20 of the Kimpton *et al.* publication read in its entirety as follows:

> The reason for the different STR frequency distributions observed here (unimodal, bimodal, and complex) is unclear. Such distributions have been reported previously for STR loci, and it was suggested that they may represent the evolutionary history of the alleles for different populations. In addition, structural limitations on allele sizes are also likely to play a major role in the generation and frequency of specific alleles.

It is submitted that, contrary to the indication in the Examiner's Answer, the Kimpton *et al.* publication neither disclosed nor in any way suggested or implied any connection between the disclosure in the first partial paragraph of column 2 on page 20 of the publication that the accuracy and reliability of the detection and sizing protocols used for allele designation with respect to the two particular loci designated HUMAPOAI1 and HUMACTBP2 should be confirmed prior to routine use of these loci by forensic laboratories for the identification of individuals and the disclosure in the third paragraph beginning in column 2 of page 20 of the publication that the reason was not clear why the short-tandem-repeat frequency distributions observed exhibited different forms. The assertion in the sentence bridging pages 14 and 15 of the Examiner's Answer that the Kimpton *et al.* publication would have taught at page 20, column 2 that "some alleles are not as easily analyzed and require analysis of the distributions" was error.

For the two loci for which it was recommended that the accuracy and reliability of the detection and sizing protocols be confirmed prior to routine use by forensic laboratories in the first partial paragraph of column 2 on page 20 of the Kimpton *et al.* publication; namely, the loci designated HUMAPOAI1 and HUMACTBP2; the publication disclosed at page 16, column 2, line 16 through column 3, line 14 and page 19, column 3, line 56 through page 20, column 1, line 4 that variability between polyacrylamide gels did not allow reliable allele designation with respect to those two loci even though differences between allele bands were readily resolvable on the gels. Nonetheless, as discussed in the Appeal Brief, allele designation could be accomplished for the HUMAPOAI1 and HUMACTBP2 loci according to the Kimpton *et al.* publication by running an allelic-ladder control on each gel for the two loci. Thus even for the HUMAPOAI1 and HUMACTBP2 loci for which variability between gels did not allow reliable allele designation, the Kimpton *et al.* publication did not suggest that any alternative method was needed to resolve the allele bands for the two loci, but disclosed that satisfactory allele designation could be accomplished with the computer-generated band-sizing technology used for the other loci by direct comparison to allelic-ladder controls run on each gel. The first partial paragraph of column 2 on page 20 of the publication called for confirmation of the accuracy and reliability of the detection and sizing protocols for the HUMAPOAI1 and HUMACTBP2 loci prior to routine use by forensic laboratories for the identification of individuals.

As persons of ordinary skill in the art would have appreciated in view of the discussion at page 17, column 1 of the Kimpton *et al.* publication of the shapes of the allele frequency histograms of Figure 3 of the publication, the reference to observed short-tandem-repeat frequency distributions in the third paragraph beginning in column 2 of page 20 of the publication would have been understood by such persons to be a reference to the allele frequency histograms depicted in Figure 3. As discussed above in connection with the new claim chart of the Examiner's Answer, that the x-axis of the allele frequency histograms of Figure 3 of the Kimpton *et al.* publication represented an "allele designation number," not an experimental electrophoretic band size, and the y-axis of the histograms represented an allele frequency. Thus a process of assigning named allele designations for each of the individuals of the populations

based on measured electrophoretic band size measurements had to have been carried out prior to compiling the allele frequency data plotted in Figure 3 of the Kimpton *et al.* publication. Furthermore, as persons of ordinary skill in the art would have recognized, it would not have been possible to deconstruct an allele frequency histogram of Figure 3 of the publication to retrieve a particular measured electrophoretic band size for a particular individual who had been assigned a given allele designation number on the basis of a measured electrophoretic band size.

The attorneys for the applicants maintain their position explained in the Appeal Brief of 17 November 2006 that a person of ordinary skill purporting to use the analytical method disclosed in the Kimpton *et al.* publication who looked for an alternative method to determine allele sizes involving some sort of continuous allele distribution model would have been going against the plain disclosure of the publication read as a whole. For the reasons set forth above, it is submitted that the two passages at column 2, page 20 of the of the publication cited in the paragraph bridging pages 14 and 15 of the Examiner's Answer would not have suggested to or motivated a person of ordinary skill in the art purporting to use the analytical method of the Kimpton *et al.* publication to look for an alternative method to determine allele sizes involving some sort of continuous allele distribution model as proposed in the final Office Action on appeal and further that the passage at page 20, column 3 of the publication cited in the paragraph bridging pages 14 and 15 of the Examiner's Answer, when taken in its entirety as required under applicable court of appeals precedent cited in the Appeal Brief as opposed to the truncated form quoted in the Examiner's Answer, would have reinforced other disclosures in the publication that the allele-designation method disclosed in the publication provided all the resolution and accuracy needed in the automated DNA profiling system of the publication.

A.1.e Ledwina *et al.* Publication Neither Disclosed Nor Suggested any Procedure for Conditional Probability Analysis of a Particular Genotype of an Individual

Regarding the Ledwina *et al.* publication, in the paragraph bridging pages 16 and 17 of the Examiner's Answer it was asserted that

> the sole issue is the probability distribution of "random vector X", which could be either the population of individuals or the population of measured alleles in an experimental situation. If the latter population is analyzed, it will result in the conditional probability of the particular genotype of an individual.

Nowhere in the Examiner's Answer is there a citation to a passage in the Ledwina *et al.* publication which supports the assertion in the Answer that the random vector **X** of the publication could specify "the population of measured alleles in an experimental situation."

The Ledwina *et al.* publication was a mathematically oriented report which made extensive use of algebraic symbols. In the first paragraph of section 1 on page 161 of the publication it was indicated that derivation of the report involved a random sample from a diploid population. In the first paragraph of section 1, the symbols $A_1, A_2,\ldots,A_m$ were defined as representing the m alleles at a certain locus. The symbol A_iA_j was defined the first paragraph of section 1 as representing an individual which resulted from the union of an A_i sperm and an A_j egg. In the first sentence of section 2 on page 162 of the Ledwina *et al.* publication, the symbol **X** was identified as the random vector $(X_{11},X_{12},\ldots,X_{mm})$ of the observed numbers of individuals A_iA_j, $i,j = 1,2,\ldots,m$.

Note that under the definition of the Ledwina *et al.* publication, each of the symbols $A_1,A_2,\ldots,A_m$ represented an allele and thus each symbol A_k corresponded to a name designating an allele, as a person of ordinary skill in the art would have recognized. Likewise, a person of ordinary skill in the art would have recognized that each symbol A_iA_j in the Ledwina *et al.* publication represented a diploid individual with a genotype specified by the two symbolically named alleles A_i and A_j. In contrast, each random-variable component X_{ij} of the random vector **X** was defined in the Ledwina *et al.* publication as representing the number of individuals in a population sample with the genotype designated by the symbol A_iA_j. Evaluating the random vector **(X=x)** in the case of a given sample of individuals randomly selected from a particular population would have been understood to entail obtaining data separately enumerating the aggregate number of individuals having each different genotype in the sample. Compiling a set

of data enumerating the aggregate number of individuals from a sample having each different genotype with respect to a genetic locus requires that the genotype of each individual in the sample be determined. The data so compiled would not have reflected the particular method by which the genotype of any individual may have been determined. For example, in evaluating the random vector **(X=x)** in the case of a given sample of individuals randomly selected from a particular population, the data enumerating the aggregate number of individuals having each different genotype in the sample would be the same even if the genotype of different individuals had been determined by entirely different experimental methods.

On page 27 of the Appeal Brief an imaginary thought experiment was described which, it is submitted, conclusively refuted the notion that the probability distributions of the Ledwina *et al.* publication could have been used somehow to determine the genotype of an individual subject, as asserted in the Examiner's Answer and in the Office Action on appeal. In particular, it was noted that the aggregate number of individuals specified by the components of the random vector **X** and the related random vectors **T** and **Z** of the various probability distributions of the Ledwina *et al.* publication would have remained invariant had any pair of individuals in the sample having different genotypes somehow magically swapped genotypes with one another with respect to some locus, and consequently any probabilities from probability distributions that were a function of such random vectors of aggregate numbers would have necessarily remained unchanged under such a genotype swap, demonstrating that such probability distributions were useless for determining the respective genotypes of individual subjects in samples with more than one genotype. No mention was made in the Examiner's Answer of imaginary thought experiment described in the Appeal Brief.

For the reasons set forth above, it is submitted that the assertion in the paragraph bridging pages 16 and 17 of the Examiner's Answer that the Ledwina *et al.* publication in some unspecified way disclosed a procedure for conditional probability analysis of a particular genotype of an individual is untenable.

A.1.f Method of Claims 96 and 106 Distinct from Any Combination of the Kimpton *et al.* Publication, the Ledwina *et al.* Publication, and the Jeanpierre Publication

In the first full paragraph on page 17 of the Examiner's Answer, it was asserted that it had been argued in the Appeal Brief of 17 November 2006 that independent claims 96 and 106 differed from the combination of the Kimpton *et al.* publication, the Ledwina *et al.* publication and the Jeanpierre publication because of the use of the phrase "genotypic classes" in the claims. The Examiner's Answer mischaracterized and trivialized the discussion regarding claims 96 and 106 in the Appeal Brief. The attorneys for the applicants stand by the analysis of claims 96 and 106 set out in the Appeal Brief, which for conciseness will not be repeated here.

A.2 The Rejection Under 35 U.S.C. § 112, Second Paragraph

In the Examiner's Answer, it was asserted that the expression "including such amplification by a polymerase chain reaction or a ligase chain reaction" in the expression "assaying for the given allele using genetic bit analysis, allele-specific hybridization, or allele-specific amplification, including such amplification by a polymerase chain reaction or a ligase chain reaction" recited in the claim was "insolubly ambiguous."

The attorneys for the applicants maintain that the antecedent basis of "including such amplification" in the immediately preceding term "allele-specific amplification," the only prior use of the word "amplification" in claim 94 and in parent claim 75, would have been immediately recognized by a person of ordinary skill in the art as a matter of basic English-language sentence construction and that the claim as presently worded is entirely clear and definite.

The authorities cited in the Examiner's Answer in support of the assertion of insoluble ambiguity are, it is submitted, significantly less germane with respect to this matter than the *MercExchange* v. *eBay* case cited in section VII.b) on page 55 of the Appeal Brief.

It is maintained that the final rejection of claim 94 under 35 U.S.C. § 112, second paragraph, was unwarranted and should be reversed.

A.3 Full Support for the Claims of the Subject Application Is Provided by Claimed Parent Application 08/173,173

In the seventh paragraph on page 2 of the Office Action on appeal, the claim of priority of the subject application back to application 08/173,173, filed 23 December 1993 ("the '173 application") and certain earlier applications was noted. It was asserted that it could not be determined whether the applications in question provided support for the current claims of the subject application and the claims were given the effective date of the immediate parent application 09/088,820, filed 2 June 1998 ("the '820 application").

In the Appeal Brief of 17 November 2006 it was noted that the pending claims of the subject application found full support in the '173 application as filed and that each claim was entitled to the benefit of the 23 December 1993 filing date of the '173 application.

The claim of priority of the subject application back to application the '173 application was noted, but not addressed, in the Examiner's Answer.

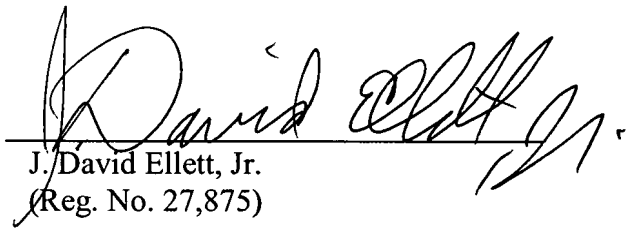
It is maintained that it was error in the Office Action on appeal to treat the claims of the subject application as limited to the filing date of the '820 application and not to accord the claims the benefit of the 23 December 1993 filing date of the '173 application for the reasons discussed in the Appeal Brief.

B. Conclusion

For the reasons set forth above and in the Appeal Brief of 17ovember 2006 it is submitted that the claims of the subject application are patentable over the art of record considered alone or in any combination and fully meet the standards of 35 U.S.C. § 112, second paragraph, and that the claims of the application find full support in claimed parent application 08/173,173. Reversal of the final rejections, affirmation of the support of the claims by parent application 08/173,173, and allowance of the application is therefore earnestly solicited.

Respectfully submitted,

Attorneys for the Applicants

by: 

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